Diabetic Proximal Neuropathy: Therapy and Prognosis

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Diabetic proximal neuropathy goes by a bewildering variety of names: diabetic femoral neuropathy, amyotrophy, neuropathic cachexia, anterior neuronopathy, polyradiculopathy, myopathy, mononeuritis multiplex or lumbar plexopathy. We are all familiar with the typical syndrome in elderly in Type 2 diabetics who develop severe unilateral anterior thigh pain followed by wasting and weakness of the quadriceps muscle with loss of the knee jerk [1]. This soon becomes bilateral in roughly 50 per cent of patients.

The underlying pathogenic mechanisms have not yet been identified. It is presumed that peripheral nerve infarcts are responsible for those cases which develop acutely over a few days. However, an earlier report of small peripheral nerve infarcts in an autopsy study [2] has been tempered by subsequent recognition that such lesions can be difficult to distinguish from Renaut bodies, a non-specific histopathological finding [3]. Furthermore, any theory that proximal diabetic neuropathy represents nerve infarction due to diabetic microvascular disease would have to account for the rarity with which it is accompanied by diabetic retinopathy or nephropathy, [4] the excellent recovery achieved by many patients, and the marked tendency for abnormalities to develop symmetrically on the two sides within a few weeks of one another [4, 5]. The other end of the clinical spectrum is less well recognized: symmetrical proximal muscle weakness of slow onset, which is relatively painless and is presumed to be metabolic in origin [6-8].

A paper in this issue of the journal by Coppack and Watkins [5] addresses two important issues concerning the treatment and prognosis of diabetic proximal neuropathy. First, does hypoglycaemic therapy really aid recovery of the leg weakness? Second, to what extent do these patients ultimately recover from disability which may be seriously incapacitating for many months?

There is no doubt that many patients with diabetic proximal neuropathy do recover. Few physicians can resist the temptation to improve glycaemic control in patients who develop diabetic proximal neuropathy and most feel this action is responsible for recovery when it occurs. But is hypoglycaemic therapy itself really responsible for recovery, or is recovery merely part of the natural history of diabetic proximal neuropathy? Garland [9] stated that 'the only treatment necessary is full diabetic control... the use of insulins is almost invariably essential' a view supported by Casey and Harrison [10]. However it is clear that diabetic proximal neuropathy can develop in patients with rather mild glucose intolerance, and that recovery can coincide merely with the institution of a low calorie diet, without additional hypoglycaemic medication [7, 10].

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Coppack and Watkins identified eight patients out of a total of 27 who were already on insulin when they developed diabetic proximal neuropathy. Indeed three of these developed diabetic proximal neuropathy despite having started insulin during the preceding one to four months because of poor glycaemic control. Insulin was commenced when diabetic proximal neuropathy was diagnosed in another eight patients; but these recovered no more quickly than others who were never treated with insulin. Taken together these observations raise doubts as to the efficacy of insulin, or other hypoglycaemic drug treatment, in securing recovery from proximal diabetic neuropathy. This question will remain unresolved because of the difficulties of mounting a trial of an established therapy which is justifiably used in the treatment of other aspects of diabetes in patients with proximal neuropathy. The practical advice to those managing proximal diabetic neuropathy must be to institute whatever measures are generally necessary to reduce hyperglycaemia but to retain an open mind about the influence of these measures in achieving neurological recovery.

In 1960, Garland stated that 'this syndrome (diabetic amyotrophy) is totally reversible'[9]. Has subsequent experience justified this euphoric view? In previous studies, many patients were followed up merely for months, rather than the periods in excess of three years that would be required to assess the slow recovery from diabetic proximal neuropathy [4, 7, 10]. Now Coppack and Watkins have reviewed hospital case records of 27 patients covering periods of 1–14 years following their diagnosis of diabetic proximal neuropathy. This showed that the severe anterior thigh pain characteristic of the condition starts to improve after a median period of 3 months and that this distressing symptom eventually clears completely in all patients. However milder residual thigh discomfort can take up to 3½ years to resolve. They personally re-examined 18 patients at a median of 45 months following diagnosis and found that 62 per cent still had mild thigh muscle weakness or residual pain and stiffness of the thighs, particularly on exercise. Less than 45 per cent of patients had made a full functional recovery. Recurrent episodes occurred in up to 20 per cent of patients. Their study did not include patients with painless symmetric proximal muscle weakness, and so we do not know whether both clinical extremes of the syndrome recover to similar degrees.

Proximal diabetic neuropathy is a seriously disabling condition, predominantly affecting the elderly, from which less than half recover fully. Although the others fortunately recover from their initial severe pain, they are left with varying degrees of disability due to residual weakness or discomfort. If recovery does occur it is protracted over many months. Relapses occur. In my opinion hypoglycaemic drugs have not been proven to promote recovery, yet commonsense indicates that such therapy should be prescribed.

REFERENCES